~~APPROVED~~ ~~DRAFT~~ PA Criteria

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CRITERIA FOR PRIOR AUTHORIZATION

Spinal Muscular Atrophy (SMA) Agents

BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES ~~T~~Prior authorization will be required for all current and future dose forms available. All medication specific criteria, including drug specific indications, age, and dose for each agent is defined in Table 1 below. ~~he following drugs requires prior authorization:~~

Nusinersen (Spinraza®)
Onasemnogene (Zolgensma®)
Risdiplam (Evrysdi™)

CRITERIA FOR INITIAL APPROVAL FOR ~~NUSINERSEN~~ SMA AGENTS (Must meet the following criteria):

- Must be approved for the indication, age, and not exceed dosing limits listed in Table 1.
- Must be prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]
- Patient must have a diagnosis of spinal muscular atrophy (SMA), confirmed by SMN1 (chromosome 5q) gene mutation or deletion.[1,2,4] Must meet one of the following:
  - Homozygous SMN1 gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13)[4,9]
  - Compound heterozygous SMN1 mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2])[9]
- Prescriber must submit baseline documentation of one of the following:[6,8-10]
  - Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)
  - Hammersmith Functional Motor Scale Expanded (HFMSE)
  - Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)
  - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
  - Current status on motor milestones: ability to sit or ambulate.
  - Motor Function Measure 32 (MFM32).
- Patient must not be on concurrent combination therapy with more than one of the following: Evrysdi (risdiplam), Spinraza (nusinersen) or Zolgensma (onasemnogene).[5]
- Patient is not on permanent ventilation (≥ 16 hours/day for > 21 days in the absence of an acute reversible event or tracheostomy).[8-10]
- If the request is for Evrysdi (risdiplam) or Spinraza (nusinersen): Provider must submit documentation the patient has a sufficient number of copies of SMN2 gene defined as ≥ 2 copies of SMN2 gene.[1,2]

~~Prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]~~

- If the request is for Evrysdi (risdiplam):
  - Patient must have symptoms of SMA.[11]
  - Patient must not have previously received Zolgensma (onasemnogene).[5]
  - Patient must meet ONE of the following:
    - Must not initiate on oral albuterol therapy during the initial approval.[6]
    - Must be stable and compliant on oral albuterol therapy for at least 6 months.[6,7]
- If the request is for Spinraza (nusinersen):
  - Must be administered by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.[8]

- Patient must not have previously received Zolgensma (onasemnogene).[5]

- If the request is for Zolgensma (onasemnogene):
  - Patient must have bi-allelic mutations in the SMN1 gene.
  - Patient must have genetic testing that confirms the absence of c.859G>C modification on exon 7.
  - Patient must be < 2 years of age. For patients born prematurely, the corresponding full gestational age must be reached prior to administration.[9]
  - If replacing Evrysdi (risdiplam) or Spinraza (nusinersen), Zolgensma (onasemnogene) will not be prescribed concurrently as dual therapy.[5]
  - Patient must not have previously received Zolgensma (onasemnogene).[9]
  - Patient must have baseline laboratory tests demonstrating anti-AAV9 antibody titers ≤ 1:50 as determined by ELISA binding immunoassay.[4,9]
  - ~~Patient must not have advanced SMA (i.e., complete paralysis of limbs, permanent ventilator dependence).[9]~~
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- ~~Prescriber must submit baseline documentation of one of the following:[6,8-10]~~
  - ~~Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)~~
  - ~~Hammersmith Functional Motor Scale Expanded (HFMSE)~~
  - ~~Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)~~
  - ~~Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)~~
  - ~~Current status on motor milestones: ability to sit or ambulate.~~
  - ~~Motor Function Measure 32 (MFM32).~~
- ~~Must be administered by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.[8]~~
- ~~Dosing must not exceed 12 mg. There are 4 loading doses. The first three loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose.[8]~~
- ~~Patient must not be on concurrent combination therapy with more than one of the following: Evrysdi (risdiplam), Spinraza (nusinersen) or Zolgensma (onasemnogene).[5]~~
- ~~Patient is not on permanent ventilation (≥ 16 hours/day for > 21 days in the absence of an acute reversible event or tracheostomy).[8-10]~~

LENGTH OF INITIAL APPROVAL

- Evrysdi (risdiplam) or Spinraza (nusinersen): 12 months
- ~~Spinraza (nusinersen): 126 months (1 loading dose [4 injections] and 1 maintenance dose.[8]~~
- Zolgensma (onasemnogene): 1 month (1 infusion per lifetime). Reauthorization is not permitted.[9]

~~6 months (1 loading dose [4 injections] and 1 maintenance dose)~~

CRITERIA FOR RENEWAL APPROVAL FOR NUSINERSEN OR RISDIPLAM (Must meet the following criteria):

- The patient continues to meet initial criteria.
- Must meet one of the following:
  - Prescriber attests that the patient has achieved a new motor milestone or maintained muscle function compared to pretreatment baseline when they would otherwise be unexpected to. ~~do so (e.g., sit unassisted, stand, walk)~~Must have one or more of the following:
    - Gains ability to sit without support ≥ 5 seconds.[10]
    - Gains ability to ambulate without support
  - ~~~~
  - Prescriber submits post-treatment documentation with the most recent results (< 1 month prior to request) documenting a positive clinical response from pretreatment baseline status demonstrated by at least one of the following:[8-10]
    - Hammersmith Infant Neurological Exam (HINE) (infant to early childhood):

- Improvement or maintenance of previous improvement of at least 2 point (or maximal score) increase in ability to kick or Improvement or maintenance of previous improvement of at least 1-point increase in any other HINE milestone (e.g., head control, rolling, sitting, crawling, etc.).~~,~~
- Hammersmith Functional Motor Scale Expanded (HFMSE):
  - Improvement or maintenance of previous improvement of at least a 3-point increase in score from pretreatment baseline.
- Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)
  - Improvement or maintenance of previous improvement of at least a 2-point increase in score from pretreatment baseline.
- Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
  - Improvement or maintenance of previous improvement of at least a 4-point increase in score from pretreatment baseline.

~~New motor milestones achieved (must have one or more of the following):~~

- ~~Gains ability to sit without support ≥ 5 seconds.[10]~~
- ~~Gains ability to ambulate without support~~

- Motor Function Measure 32 (MFM32):
  - Improvement or maintenance of previous improvement of at least a 3-point increase in score from pretreatment baseline.[10]

- ~~Dosing must not exceed~~ the FDA-approved dose as listed below in Table 1. ~~12 mg. A maintenance dose should be administered once every 4 months.[8]~~
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LENGTH OF RENEWAL APPROVAL~~—~~

~~Evrysdi (risdiplam)~~: 12 months

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FOR DRUGS THAT HAVE A CURRENT PA REQUIREMENT, BUT NOT FOR THE NEWLY APPROVED INDICATIONS, FOR OTHER FDA-APPROVED INDICATIONS, AND FOR CHANGES TO AGE REQUIREMENTS NOT LISTED WITHIN THE PA CRITERIA:
THE PA REQUEST WILL BE REVIEWED BASED UPON THE FOLLOWING PACKAGE INSERT INFORMATION: INDICATION, AGE, DOSE, AND ANY PRE-REQUISITE TREATMENT REQUIREMENTS FOR THAT INDICATION.

- ~~Spinraza (nusinersen): 12 months (3 maintenance doses)~~
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~~**CRITERIA FOR APPROVAL FOR ONASEMNOGENE** (Must meet the following criteria):~~

- ~~Patient must have a diagnosis of spinal muscular atrophy (SMA).[4]~~
  - ~~Genetic testing confirms the presence of homozygous mutation in the SMN1 gene (e.g., biallelic deletions of exon 7).[4,9]~~
  - ~~Genetic testing confirms that member does not have a single base substitution in SMN2 gene (c.859G>C modification on exon 7).[9]~~
- ~~Prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]~~
- ~~Patient must have symptoms prior to 6 months of age.[9]~~
- ~~Patient must be < 2 years of age.[9]~~
- ~~For patients born pre-maturely, Zolgensma (onasemnogene) cannot be administered until the corresponding full gestational age is reached.[9]~~
- ~~If replacing Spinraza (nusinersen), Zolgensma (onasemnogene) will not be prescribed concurrently as dual therapy.[5]~~
- ~~Patient must not have previously received Zolgensma (onasemnogene).[9]~~
- ~~Prescriber must submit baseline documentation of one of the following:~~
  - ~~Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)~~
  - ~~Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)[6]~~
- ~~Patient must have baseline laboratory tests demonstrating Anti-AAV9 antibody titers ≤ 1:50 as determined by ELISA binding immunoassay.[4,9]~~
- ~~Patient must not have advanced SMA (i.e. complete paralysis of limbs, permanent ventilator dependence).[9]~~
- ~~Patient must not require permanent ventilation, tracheostomy, or non-invasive ventilation beyond use for sleep (requiring invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in the absence of an acute reversible illness, excluding perioperative ventilation).[9]~~
- ~~Total dose must not exceed 1.1 x 10^{14} vector genomes (vg) per kilogram (kg).[9]~~

~~**LENGTH OF INITIAL APPROVAL** 1 month (1 infusion per lifetime). Reauthorization is not permitted.[9]~~

~~**CRITERIA FOR INITIAL APPROVAL FOR RISDIPLAM** (Must meet the following criteria):~~

- ~~Patient must have a diagnosis of spinal muscular atrophy (SMA), confirmed by SMN1 (chromosome 5q) gene mutation or deletion.[10]~~
- ~~Patient must have symptoms of SMA.[11]~~
- ~~Provider must submit documentation the patient has a sufficient number of copies of SMN2 gene defined as ≥ 2 copies of SMN2 gene.[10]~~
- ~~Prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]~~
- ~~Prescriber must submit baseline documentation of one of the following:[8,10]~~
  - ~~Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)~~
  - ~~Hammersmith Functional Motor Scale Expanded (HFMSE)~~
  - ~~Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)~~
  - ~~Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)~~
  - ~~Current status on motor milestones: ability to sit or ambulate.[10]~~
  - ~~Motor Function Measure 32 (MFM32).[10]~~

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- ~~Dosing must not exceed any of the following total daily doses:[10]~~
  - ~~Age 2 months to 2 years: 0.2mg/kg.~~
  - ~~Age > 2 years and weighing < 20kg: 0.25mg/kg.~~
  - ~~Age > 2 years and weighing ≥ 20kg: 5mg.~~
- ~~Patient must not have previously received Zolgensma (onasemnogene).[5]~~
- ~~Patient must not be on concurrent combination therapy with Zolgensma (onasemnogene) nor Spinraza (nusinersen).[5]~~
- ~~Patient must meet ONE of the following:~~
  - ~~Must not initiate on oral albuterol therapy during the initial approval.[6]~~
  - ~~Must be stable and compliant on oral albuterol therapy for at least 6 months.[6,7]~~
- ~~Patient is not on permanent ventilation (≥ 16 hours/day for > 21 days in the absence of an acute reversible event or tracheostomy).[10]~~

~~**LENGTH OF INITIAL APPROVAL** 12 months~~

~~**CRITERIA FOR RENEWAL APPROVAL FOR RISDIPLAM** (Must meet the following criteria):~~

- ~~The patient continues to meet initial criteria.~~
- ~~Must meet one of the following:~~
  - ~~Prescriber attests that the patient has achieved a new motor milestone or maintained muscle function compared to pretreatment baseline when they would otherwise be unexpected to do so (e.g., sit unassisted, stand, walk)~~
  - ~~Prescriber submits post-treatment documentation with the most recent results (< 1 month prior to request) documenting a positive clinical response from pretreatment baseline status demonstrated by at least one of the following:[8,10]~~
    - ~~Hammersmith Infant Neurological Exam (HINE) (infant to early childhood):~~
      - ~~Improvement or maintenance of previous improvement of at least 2 point (or maximal score) increase in ability to kick or Improvement or maintenance of previous improvement of at least 1 point increase in any other HINE milestone (e.g., head control, rolling, sitting, crawling, etc.),~~
    - ~~Hammersmith Functional Motor Scale Expanded (HFMSE):~~
      - ~~Improvement or maintenance of previous improvement of at least a 3 point increase in score from pretreatment baseline~~
    - ~~Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)~~
      - ~~Improvement or maintenance of previous improvement of at least a 2-point increase in score from pretreatment baseline~~
    - ~~Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)~~
      - ~~Improvement or maintenance of previous improvement of at least a 4-point increase in score from pretreatment baseline~~
    - ~~New motor milestones achieved (must have one or more of the following):~~
      - ~~Gains ability to sit without support ≥ 5 seconds.[10]~~
      - ~~Gains ability to ambulate without support.~~
    - ~~Motor Function Measure 32 (MFM32).[10]~~
      - ~~Improvement or maintenance of previous improvement of at least a 3-point increase in score from pretreatment baseline.~~
- ~~Dosing must not exceed the FDA-approved dose as above.~~

~~**LENGTH OF RENEWAL APPROVAL** 12 months~~

Notes:

- Efficacy of risdiplam in pre-symptomatic SMA patients is actively being studied.[11]

Table 1. FDA-approved age and dosing limits for SMA Agents.[8-10]

Agents	Indication(s)	Age	Dosing Limits
Antisense Oligonucleotides			
Nusinersen (Spinraza®)	Treatment of spinal muscular atrophy	Newborn - adult	4 Loading doses: 12 mg intrathecally. The first 3 loading doses should be administered at 14- day intervals; the 4th loading dose should be administered 30 days after the 3rd dose. Maintenance dose: 12 mg intrathecally administered once every 4 months.
Adeno-associated Virus Vector-based Gene Therapy			
Onasemnogene (~~Zolgenesma~~Zolgensma®)	Treatment of s~~S~~pinal muscular atrophy	< 2 years	1.1 x 10^{14} vector genomes (vg) per kg of body weight.
Survival of Motor Neuron 2 (SMN2)-Directed RNA Splicing Modifier			
Risdiplam (Evrysdi™)	Treatment of spinal muscular atrophy	≥ 2 months	2 months to < 2 years of age: 0.2 mg/kg orally once daily. ≥ 2 years and weighing < 20 kg: 0.25mg/kg orally once daily. ≥ 2 years and weighing ≥ 20 kg: 5 mg orally once daily.

Table 2~~1~~. Types of spinal muscular atrophy (SMA).[3]

SMA Type	Highest motor function without treatment*
1	Unable to sit independently
2	Able to sit, never able to walk independently
3	Able to walk independently

*SMA Types are classified based on the highest motor milestone attained.[3]

References:

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9. Zolgensma (onasemnogene abeparvovec) [prescribing information]. Bannockburn, IL: AveXis, Inc; May 2019.
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DRUG UTILIZATION REVIEW COMMITTEE CHAIR	PHARMACY PROGRAM MANAGER DIVISION OF HEALTH CARE FINANCE KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT
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